UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,833	12/02/2003	Thomas Nelson	17357.01302US	2811

38647 7590 02/22/2005

MILBANK, TWEED, HADLEY & MCCLOY LLP
INTERNATIONAL SQUARE BUILDING
1825 EYE STRET, N.W. #1100
WASHINGTON, DC 20006

EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 02/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/724,833	NELSON ET AL.	
	Examiner	Art Unit	
	Agnes B Rooke	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *34-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33 and 39-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *Dec 15, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I, Claims 1-27 and 39-41 in the reply filed on December 13, 2004, is acknowledged. The traversal is on the grounds that the search and/or examination of the claimed subject matter of Group I and Group II, and a search of apolipoprotein and therapeutic agent genuses would not impose a serious burden on the examiner. Therefore, the argument is found persuasive and the examiner rejoined Group I and Group II and withdrawn the election of species requirement.

Therefore, Claims 1-41 are pending.

Claims 34-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups. Claims 1-33 and 39-41 are currently under examination.

A complete reply to the final rejection must include cancellation of the nonelected claims or other appropriate action (37 CFR 1.144) See MPEP paragraph 821.01.

Objections to Claims

The name of "LDL" in the first claim must be spelled out.

Objections to Specification

Page 25, [00104] of the specification, states that *"LDL suspension is stable for at least 7..."* The time frame for the stability of suspension must be specified.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 2, 3, 5, 6, 10, 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants use the phrase *"at least"* where referring to apolipoproteins, therapeutic agents or uptake specificity. Instead of using the phrase *"at least"* the Applicants should provide a particular number or a numerical range. Therefore, the appropriate corrections are required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-17, 22-27, and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Versluis et al., Stable Incorporation of a Lipophilic Danorubicin Prodrug into Apolipoprotein E-Exposing Liposomes Induces Uptake

of Prodrug via Low-Density Lipoprotein Receptor in Vivo, J. Pharmacol. Exp. Ther., (1999), 289(1), p. 1-7.

Egg yolk phosphatidylcholine (EYPC) cholesteryl oleate (Claim 4), and LAD (Claim 5 and 7) were sonicated and the liposomes isolated (Claim 1). The liposomes were provided with ApoE3 by incubating the particles just before use, resulting in an APOE3/phospholipids ratio of 0.1:1 (w/w) (Claims 2, 3, 9, 10).

The density of the particles was 1.016 to 1.040 g/ml (Claims 13 and 14). The particle size was 29.3 nm (Claims 11 and 12). See page 3, right column.

The daunorubicin is linked to cholesteryl-oleate via a tetrapeptide spacer (Claims 6 and 8).

The serum half-life was enforced and the LAD was still completely associated with the liposome. See page 4, right column. Therefore, the serum stability can be said to be greater than 2 hours (Claim 15).

Versluis et al. did not assess brain uptake of LAD in ApoE3 enriched liposomes. However, because the liposomes claimed are the same as those taught in Versluis et al., then it is inherent that the liposome crosses the blood brain barrier. (Claims 16, 17, 22-24, 25-27, and 39-41).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 18, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Versluis et al. in view of Westesen et al., Characterization of native and Drug-Loaded Human Low Density Lipoproteins, J. of Pharmaceutical Sciences (1995), vol. 84, p. 139-147.

The teachings of Versluis et al. are discussed above. Versluis et al. do not teach an artificial LDL particle and conjugate between cholesterol and adriamycin.

Westesen et al. teach conjugate of cholesterol and adriamycin incorporated into LDL particle. See Abstract, and Table 4, page 141.

Therefore, it would have been obvious for a person of ordinary skill in the art to combine the artificial LDL particle of Versluis et al. with conjugate of adriamycin and cholesterol of Westesen et al. because Westesen et al. teach

that it is a common practice to have a cholesterol conjugate with adriamycin inserted into an artificial LDL particle for efficient delivery of a drug into a targeted tissue.

Claims 1, 19, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Versluis et al. in view of Meers et al. (U.S. 6,087,325).

The teaching of Versluis et al. are discussed above. Versluis et al. do not teach an artificial LDL particle with conjugate between cholesterol and tetracycline.

Meers et al. teach liposomes with tetracycline and cholesterol for efficient delivery to mammals. See Column 9, line 25-36.

Therefore, it would have been obvious for a person of ordinary skill in the art to design artificial LDL particle of Versluis et al. with tetracycline and cholesterol of Meers et al. because Meers et al. teach that it is routine to deliver bioactive agents such as tetracycline and cholesterol to a targeted tissue of mammal for treatment.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful,

the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

AR

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER